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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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72960

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EXAMINER

MEHMOOD, SEHAR BEENA

ART UNIT

PAPER NUMBER

4118

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/559,742	Applicant(s) TAKAYAMA ET AL.	
	Examiner SEHAR MEHMOOD	Art Unit 4118	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/14/2006; 8/5/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration acknowledges the duty to disclose to the Office all information known to the person to be “material to **patentability** as defined in 37 CFR 1.56.”

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 10, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. Claim 1c recites the limitation "said downstream portion" in line 13. There is insufficient antecedent basis for this limitation in the claim.
5. Claim 1e recites the limitation "said chamber" in lines 18-20. There is insufficient antecedent basis for this limitation in the claim. Recommended change is “said oocyte insemination chamber.”
6. Claim 10 recites the limitation "said chamber" in line 9. There is insufficient antecedent basis for this limitation in the claim. Recommended change is “said oocyte insemination chamber.”

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7. Claim 12 recites the limitation "the rate of fertilization" in line 15. There is insufficient antecedent basis for this limitation in the claim.
8. Claim 12 recites the limitation "said channel" in lines 17, 20, and 23. There is insufficient antecedent basis for this limitation in the claim. Recommended change is "said microfluidic channel"
9. Claim 12 recites the limitation "the sperm concentration" in line 24. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1-2, 5-6, 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al. (US 2003/0165812) in view of Gordon (US 5,627,066).

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13. Re Claim 1, Takayama et al. discloses an integrated microfluidic sperm isolation device 1 comprising

- at least two gravity pump liquid reservoirs (paragraph [0049], line 2), one of said reservoir being a sperm receiving reservoir (motile particle supply reservoir 2; Figure 1; paragraph [0020], line 3), one of said reservoirs being a sort media liquid reservoir (media reservoir 3; Figure 1; paragraph [0020], line 4);
- at least one sort channel, said sort channel 6 (Figure 1; paragraph [0020], line 8) having a sort side (corresponding to side of media stream inlet channel 8) and a reject side (corresponding to side of sort stream inlet channel 7) (Figure 1; paragraph [0020], line 10), and an upstream portion in fluid communication with said sperm receiving reservoir on said reject side of said sort channel, and in fluid communication with at least one sort media reservoir on said sort side of said sort channel (Figure 1; paragraph [0022], lines 9-14);
- a rejected sperm receiving reservoir (motile particle-depleted sort stream reservoir 4; Figure 1; paragraph [0020], lines 5-6) in fluid communication with said downstream portion of said sort channel on said reject side of said sort channel (Figure 1);
- a sorted sperm reservoir (motile particle-enriched stream outlet 5; Figure 1; paragraph [0020], lines 6-7) in fluid communication with said downstream portion of said sort channel on said sort side of said sort channel (Figure 1), and
- sperm-containing liquid in said sperm receiving reservoir and a sort media liquid in a second reservoir exhibit gravity induced co-laminar flow of both liquids through said sort channel in parallel but separate streams having an interface therebetween,

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wherein motile sperm cross said interface and are ultimately transported in said sort media liquid to said oocyte insemination chamber from said sort channel or from said sorted sperm reservoir (Figure 2a-c; paragraph [0022]. lines 9-17).

Takayama et al. does not disclose an oocyte insemination chamber sized to contain one or more oocytes and into which sorted sperm flows, said chamber configured to contain at least one barrier which prevents egress of oocyte(s) located in said chamber but which is configured to allow fluid flow into or through said chamber, wherein said oocyte insemination chamber and said sorted sperm reservoir may together be a single chamber. Gordon teaches sperm samples 34 swimming to oocytes 33 in oocyte chambers 4, fertilizing the oocytes present (effectively causing the oocyte insemination chamber and sorted sperm reservoir becoming a single chamber) (Col 4, lines 31-33) and the oocyte chambers 4 have such shapes such as a vortex shape (Col 4, lines 43-45 and 53-54) that keeps the oocytes within a particular location while allowing the motile sperms to swim to the oocytes.

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al., to include a chamber that contains oocytes at the end of the sorted sperm stream with barriers, as taught by Gordon, in order to fertilize an oocyte in vitro in one set-up/environment.

14. Re Claim 2, Takayama et al. also discloses the device 1 being constructed of silicone elastomer (paragraph [0045], lines 3-5).

15. Re Claim 5, Gordon also teaches a barrier comprises a three dimensional barrier grate having forming plurality of barrier flow channels, said barrier flow channels smaller than an oocyte diameter by an amount such that said oocyte is blocked from passing through said barrier

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flow channels, but larger than the size of sperm such that sperm may travel through said barrier (Col 4, lines 43-45 and 53-54).

16. Re Claim 6, Takayama et al./Gordon discloses a method for in vitro insemination of an oocyte with sorted, motile sperm with minimal manipulation of said oocyte, said method comprising:

- selecting a device of claim 1;
- introducing one or more oocytes into said oocyte insemination chamber (Gordon; Col 4, line 22);
- introducing a first sperm-containing liquid to be sorted into a second sperm-containing liquid containing sperm of higher average motility than sperm of said first sperm containing liquid (Takayama et al.; paragraph [0023], lines 6-8);
- introducing a sort media liquid into said sort media liquid reservoir (Takayama et al.; paragraph [0022], lines 5-6);
- flowing said first sperm-containing liquid and said sort media liquid co-laminarly through said sort channel (Takayama et al.; paragraph [0022], lines 9-12);
- removing from said sort channel said second sperm-containing liquid (Takayama et al.; paragraph [0025], lines 1-4); and
- contacting said second sperm-containing liquid with said oocyte(s) (Gordon; Col 4, lines 31-33).

It would have been obvious at the time of the invention was made that when Takayama et al. was modified with Gordon, the resulting device of claim 1 would be able to perform the above mentioned steps due to the structure and function of the device.

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17. Re Claim 11, Takayama et al. also discloses a growth media liquid being introduced into at least one of said gravity pump liquid reservoirs to provide a flow of growth media past said fertilized oocyte(s) (Paragraph [0027], lines 1-7).

18. Re Claim 12, Takayama et al./Gordon discloses a method for improving the rate of fertilization of oocytes when employing low sperm concentration, comprising introducing one or more oocytes into a microfluidic channel, said channel having disposed therein a barrier having openings therein through which liquid and sperm may flow, but which are too small to allow an oocyte to enter (Gordon; Col 4, lines 43-45 and 53-54); introducing liquid and causing said oocyte(s) to travel through said channel to said barrier (; introducing a sperm-containing liquid of low sperm concentration into said channel and flowing said sperm-containing liquid past said oocyte(s) (Gordon; Col 4, lines 31-33), wherein the rate of fertilization at the sperm concentration used is higher than the rate achieved in center-well fertilization.

19. Re Claim 13, Takayama et al./Gordon discloses the claimed invention except for the sperm concentration is less than 0.5×10^6 sperm/mL. Gordon teaches that low sperm counts are 20×10^6 sperm/mL or substantially less (Col 9, lines 65-66). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Takayama et al./Gordon to utilize sperm counts, even those that are low, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

20. Claims 3-4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al./Gordon in view of Beebe et al. (US 6,193,647).

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21. Re Claim 3 and 4, Takayama et al./Gordon discloses all of the claimed elements, except for having an oocyte duct communicating with said oocyte insemination chamber/sorted sperm reservoir. Beebe et al. teaches a well 42 which is in fluid communication with a microfluidic channel 14 is used for the insertion or removal of embryo 16 (embryo is a fertilized oocyte, thus an oocyte can be used in place of an embryo) (Col 5, lines 62-67). Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include an oocyte duct or well, as taught by Beebe et al., for the purposes of facilitating and the introduction and removal of oocytes/embryos from any chamber or location.

22. Re Claim 7, Takayama et al./Gordon discloses all of the claimed elements, except for the method of claim 6 comprising introducing said oocyte(s) into said oocyte insemination chamber through said oocyte duct, and removing one or more sperm-contacted oocytes from said oocyte insemination chamber through said oocyte duct. Beebe et al. teaches a well 42 in fluid communication with a microfluidic channel 14, into which embryos 16 are inserted or removed (embryo is a fertilized oocyte, thus an oocyte can be used in place of an embryo) (Col 5, lines 62-67). The oocyte duct/well 42 can easily be attached to an oocyte insemination chamber and the oocytes can be introduced at the beginning of the process and removed once fertilized at the end of the process. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include an oocyte duct or well connected to an oocyte insemination chamber, as taught by Beebe et al., for the purposes of guiding the instrument inserting and removing oocytes/embryos.

23. Re Claim 8, Takayama et al./Gordon also discloses that sperm-contacted oocyte is a fertilized oocyte (Gordon; Col 4, lines 31-33).

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24. Re Claim 9, Takayama et al./Gordon discloses all of the claimed elements, except for introducing and removing of said oocyte(s) from said oocyte insemination chamber are performed with a pipette. Beebe et al. teaches inserting and removing oocytes/embryos 16 via pipette 44 (Col 6, lines 5-7). Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include the usage of a pipette, as taught by Beebe et al., in order to use an easy and convenient way for moving oocytes from location to location.

25. Re Claim 10, Takayama et al./Gordon discloses all of the claimed elements, except for the oocyte insemination chamber being configured such that a plurality of oocytes occupying said chamber are forced to assume serial positions with respect to the direction of fluid flow. Beebe et al. teaches embryo 16 being placed in a microfluidic channel 14 that has biological medium (Col 6, lines 2-4) with flow and embryos rolling and sliding along the channels in the direction of the flow (Col 8, lines 57-61). Since oocytes would be placed one at a time, the oocytes would move serially along the flow of fluid. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include a configuration within the oocyte insemination chamber, as taught by Beebe et al., for the purposes of having an organized environment in which the oocytes are fertilized.

Conclusion

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Aravanis et al. (US 6,929,945), Kricka et al. (US 5,427,946), and Mers Kelly et al. (US 6,033,358).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEHAR MEHMOOD whose telephone number is (571)270-7857. The examiner can normally be reached on Monday-Friday 9am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Quang Thanh can be reached on (571)272-4982. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SEHAR MEHMOOD/
Examiner, Art Unit 4118

/Quang D. Thanh/
Supervisory Patent Examiner, Art Unit
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